REMARKS

The Examiner is thanked for the due consideration given the application. Claims 1-25 are pending in the application. Claims 1 and 11 are independent.

No new matter is believed to be added to the application by this Response.

Rejection Under 35 USC §103(a)

Claims 1-10 and 16-25 have been rejected under 35 USC §103(a) as being unpatentable over OISHI et al. (U.S. Patent No. 6,165,363) in view of KAWATA et al. (U.S. Patent No. 5,340,480). This rejection is respectfully traversed.

The present invention pertains to providing a plasma purification membrane which 1) rarely clogs, 2) has high strength, and exhibits 3) excellent water permeability and 4) excellent fractionation performance in plasma purification using inside-out filtration (paragraph [0014] of the publication of the present application - U.S. Publication No. 2006/0108288).

A plasma purification membrane which 1) rarely clogs and 4) exhibits excellent protein separation properties when filtering a liquid or the like from the side of the hollow section of the membrane (hereinafter may be called "inside-out filtration") has not as yet been provided. This is because ***it is impossible to form a pore with a large pore size which allows plasma proteins to pass therethrough in the inner surface of the membrane having a gradient structure, in which the pore size is***

continuously decreased from the outer surface to the inner surface of the membrane, while 2) maintaining the strength of the membrane (*see* paragraph [0015] of the publication of the present application).

Extensive studies were conducted to achieve the above ***four objectives*** while 1) ***forming a gradient structure in which the pore size is continuously decreased from the outer surface to the inner surface of the membrane*** in order to prevent clogging, and 2) increasing hydrophilicity of the inner surface of the membrane with which a liquid to be filtered comes into contact so that protein or the like does not undergo hydrophobic adsorption.

As a result, ***a desired membrane was obtained by using a specific production method.*** This finding led to the completion of the present invention (*see* paragraph [0016] of the publication of the present application). The ***structure of the inventive membrane*** exhibits excellent plasma protein separation properties during inside-out filtration, the ***properties of the pores*** that exist in the inner surface of the membrane exhibit excellent performance that allows separation of useful proteins and unnecessary proteins in plasma, and the membrane ***has high strength in spite of the large pore size*** set forth in the claims.

The present invention thus pertains to a hollow fiber plasma purification membrane (a) having a sponge structure in which a pore size is continuously decreased from an outer surface to an inner surface of the membrane, and having (b) a breaking

stress of 50 kgf/cm2 or more, and (c) a total protein permeability of 50% or more and (d) an immunoglobulin (IgM) permeability of 90% or less when subjecting bovine plasma to inside-out filtration. *See* claim 1.

The pore size gradient of the membrane of the present invention can be readily observed in Figure 1 of the application, which is reproduced below.

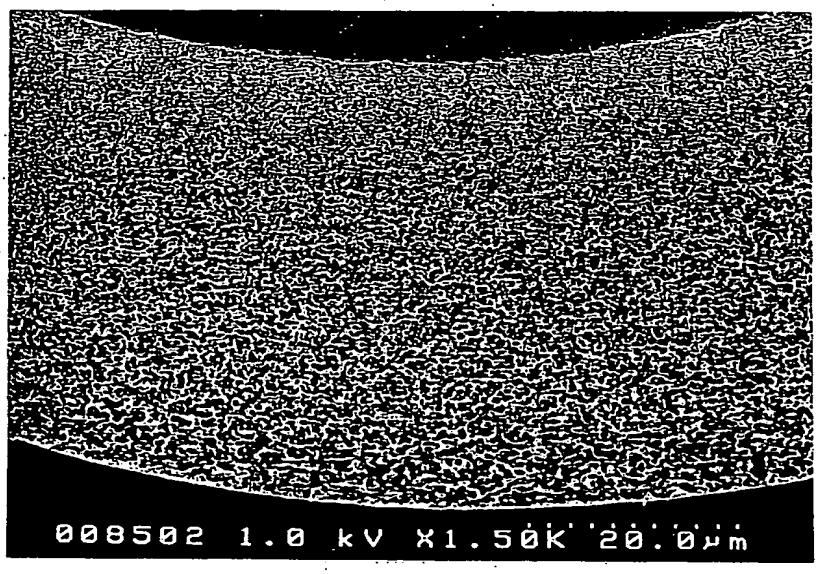


Fig. 1

The effects of the present invention are obtained by achieving the objectives of the present invention. Specifically, the plasma purification membrane according to the present invention 1) rarely clogs during plasma purification using inside-out filtration, 2) has high strength, and exhibits 3) excellent water permeability and 4) excellent fractionation performance (*see* paragraph [0149] of the publication of the present application).

OISHI et al.

The object of OISHI et al. is to provide a hollow fiber membrane having a high enough strength to withstand abrupt changes in temperature and changes in pressure at back washing and having well-balanced performances in water permeability and fractionation (*see* column 1, "DISCLOSURE OF INVENTION" of OISHI et al.).

However, the membrane of OISHI et al. has high strength and high water permeability in spite of the average pore diameter of the minimum pore diameter layer being small. Therefore, this membrane is suitable for microfiltration, especially in the field of condensation treatment in nuclear power stations and thermal power stations, the field of removal of muddiness in tap water such as potable water and processing water, and the fields of fermentation and food (*see* column 8, "INDUSTRIAL APPLICABILITY" of OISHI et al.). Specifically, the microfiltration membrane of OISHI et al. has pores larger than those of the membrane of the present invention taking its applications into consideration. This is evident from the fact that Table 1 of OISHI et al. describes that the average pore diameter of the minimum pore diameter layer is as large as 0.27 μm (Example 1) and 0.30 μm (Example 2).

Therefore, since the microfiltration membrane of the cited reference A has a large pore size, the microfiltration membrane of the cited reference A is not suitable for causing

useful proteins (albumin and γ-globulin) in plasma to permeate, and removing unnecessary proteins (IgM (immunoglobulin)) and lipids.

Accordingly, the effects and objects of the present invention clearly differ from those of OISHI et al. in that OISHI et al. fail to refer to plasma purification using inside-out filtration, and the present invention achieves excellent fractionation performance that enables separation of useful proteins and unnecessary proteins in plasma.

Also, the membrane of OISHI et al. has a configuration in which 1) the pore size is decreased from the inner surface to the outer surface of the membrane. This pore size distribution is completely the reverse of that of the present invention. Since the membrane of OISHI et al. has a pore size larger than that of the membrane of the present invention, the membrane of OISHI et al. has 2) a permeability of immunoglobulin of more than 90%. Therefore, OISHI et al. do not describe the items (a) pore size gradient, and (d) permeability of the present invention described above.

KAWATA et al.

KAWATA et al. provide polysulfone-based hollow fiber membranes having an excellent biocompatibility with a water-permeability not deteriorated after drying, which are particularly suited for blood treatment (column 3, lines 34 to 43 of KAWATA et al.).

KAWATA et al. describe that the polysulfone-based hollow fiber membrane has the following effects. Column 20, lines 36 to 65 of KAWATA et al. states:

> [T]he polysulfone-based hollow fiber membranes of the present invention comprise such hydrophilic polymers of which types, contents and configurations can provide membranes with excellent biocompatibility, particularly antithrombogenetic ability, and besides have a sharp fractionating ability. Therefore, in the body fluid treatment, for example, hemodialysis, with the hollow fiber membranes of the present invention, no or substantially no remaining blood (by clogging in the hollow fiber) is observed by virtue of an excellent antithrombogenetic ability, so that hemodialysis therapy can be conducted with safety. Alternatively, in medical treatment such as continuous hemofiltration (CAVH) wherein filtration is continuously conducted for a long time, the hollow fiber membranes of the invention can be used without clogging by thrombi even with a small dose of heparin. Further, since middle molecular weight substances can permeate but useful proteins such as albumin are not removed, the membranes of the present invention can maintain a colloid osmotic pressure. Additionally, the manufacturing processes of the polysulfone-based hollow fiber membranes according to the present invention, since the viscosity of the dopes can be easily controlled and, in addition, the content of the vinylpyrrolidone-based polymers in the skin layer on the inner surface of the hollow fiber membranes is low, the hollow fiber membranes do not stick to each others during manufacturing so that they can be produced with stability.

Therefore, the objective of KAWATA et al. is to use the hollow fiber membranes for hemodialysis. KAWATA et al. describe that useful proteins such as albumin are removed by the hollow fiber membranes to only a small extent (i.e., albumin does not permeate the membranes).

On the other hand, since the membrane of the present invention allows albumin (i.e., useful proteins) to permeate (paragraphs [0067] and [0068] of the publication of the present application), it is clear that the hollow-fiber membrane of KAWATA et al. has a pore diameter considerably smaller than that of the membrane of the present invention. Accordingly, the hollow fiber membrane of KAWATA et al. does not allow immunoglobulin having a molecular weight higher than that of albumin to permeate. Moreover, the cited reference B does not teach the structure and the strength of the membrane of the present invention.

Therefore, the present invention differs from the cited reference B as to the effects 1), 2), and 4) regarding the effects of the present invention described above.

That is, the hollow fiber membranes of KAWATA et al. have many microslits of a 0.001-0.05 μm slit-width in the inner surface and micropores of a 0.05-1 μm pore diameter in the outer surface layer. Besides, the membranes have an asymmetrical cross-sectional structure formed of:

a dense skin layer 0.1-3 μm thick on the inner surface for separating substantially substances from filtrates, which contains micropores having a pore diameter gradually increasing toward a core layer supporting the skin layer; and

a supporting core layer of has a reticular texture having micropores of a 1-5 μm average pore diameter in which the

pore diameter gradually increases toward the core layer in the thickness direction (column 3, lines 23 to 36 of KAWATA et al.).

Therefore, since the membranes of KAWATA et al. have a structure in which the pore size gradually increases from each surface to the center, the structure of the membranes of KAWATA et al. differs from the structure of the present invention in which the pore size continuously decreases from the outer surface to the inner surface.

Therefore, the hollow-fiber membrane of KAWATA et al. does not allow albumin to permeate. The hollow-fiber membrane of the cited reference B thus has a total protein permeability of 0% and an immunoglobulin permeability of 0%. KAWATA et al. fail to refer to plasma protein permeability and plasma purification.

The Office Action asserts that "the membrane in Kawata et al. has the immunoglobulin retention of less than 90% as in claim 1 (see column 10, last paragraph bridging column 11)". However, only β-thromboglobulin is referred to in that portion of the cited reference B. β-thromboglobulin (molecular weight: 35,000) is a protein smaller than albumin.

Furthermore, KAWATA et al. do not describe that the membrane has a breaking stress of 50 kgf/cm^2 or more.

Therefore, KAWATA et al. fail to describe the items (a) to (d) regarding the configuration of the present invention described above and set forth in claim 1.

Accordingly, combining OISHI et al. with KAWATA et al. would fail to have one of ordinary skill and creativity provide a) plasma purification using inside-out filtration and b) excellent fractionation performance that enables separation of useful proteins and unnecessary proteins in plasma, as is clear from the discussion above.

OISHI et al. and KAWATA et al. thus fail to disclose or suggest all the limitations set forth in claim 1 of the present invention. A *prima facie* case of unpatentability has thus not been made. Claims depending upon claim 1 are patentable for at least the above reasons.

This rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

Double Patenting Rejection

Claims 1-15 have been rejected under the doctrine of nonstatutory obviousness-type double patenting over claims 1-10 of U.S. Patent 7,087,168 (OISHI et al. '168). This rejection is respectfully traversed.

A terminal disclaimer of U.S. Patent 7,087,168 is being filed concurrently with this paper, thereby effectively removing U.S. Patent 7,087,168 as prior art to the present invention.

This rejection is believed to be overcome and withdrawal thereof is respectfully requested.

Conclusion

The Examiner is thanked for considering the Information Disclosure Statement filed March 14, 2005 and for making an initialed PTO-1449 Form of record in the application.

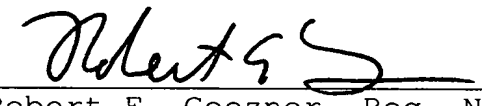
Prior art of record but not utilized is believed to be non-pertinent to the instant claims.

The rejections are believed to have been overcome, obviated or rendered moot and that no issues remain. The Examiner is accordingly respectfully requested to place the application in condition for allowance and to issue a Notice of Allowability.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



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Appendix:

The Appendix includes the following item:

- terminal disclaimer